REMARKS/ARGUMENTS

The application has been amended. In particular, claims 1 and 16 have been amended to include structural chemical formulas and other identifying characteristics for the oligourea. Claim 2 has been amended to recite "*in vitro*". The dependencies of claims 18 and 19 have been changed to depend from claim 16. Claims 5, 7-9, 17, 27 and 28 have been cancelled, and claims 29-34 have been added. Support for these amendments can be found in the application as filed.

CLAIM REJECTIONS UNDER 35 U.S.C.§ 112, FIRST PARAGRAPH

Written Description Rejection

The Examiner has rejected claims 1-5, 7-9, 16-19, 27 and 28 under 35 U.S.C.§ 112, first paragraph for containing subject matter which was allegedly not sufficiently described in the specification.

The Examiner states the following:

> **The claims of the instant application are broadly directed toward any oligourea simply comprising the basic-arginine rich region of Tat. The disclosure appears to describe a specific compound having the following structural formula set forth in Figure 1B wherein R_1 and R_2 comprise the arginine-rich region of HIV-1 set forth in Figure 1A. However, the claims fail to provide any significant structural limitations. They simply stipulate that the composition comprises an oligourea. The disclosure fails to provide any guidance pertaining to acceptable side-chain substitutions (R_1/R_2) or the length of the oligourea. Accordingly, the skilled artisan cannot readily envisage any additional molecules.**

Claim 1 is now directed to a synthesized oligourea comprising the recited structural chemical formula. As described in the application, and as now recited in claim 1, the oligourea molecule may vary in length from 3 to 50 urea-units long (page 6, lines 30-35 to page 7, lines 1 and 2). A length of 5 to 30 is more preferred (new claim 32), as described in the application. A length of 8 to 25 is most preferred (new claim 33), as described in the application. Thus, contrary to the Examiner's assertions, the disclosure does provide guidance pertaining to the length of the oligourea.

With respect to acceptable side-chain substitutions (R_1/R_2), Applicants disagree with the Examiner's assertion that the disclosure fails to provide any guidance pertaining to acceptable side-chain substitutions. As the Examiner is aware, the analysis as to whether Applicant was in possession of the claimed invention must be conducted from the standpoint of one of skill in the art. As disclosed in the application, the present invention is directed to a synthesized oligourea containing the basic-arginine rich region of Tat (see page 3, lines 5-7). It commonly known in the art that this Tat basic region corresponds to amino acids 49-57 of the naturally-occurring HIV-1 Tat protein. See, for example, the abstract of U.S. Patent No. 6,316,003, which Applicants submit as evidence of this universal fact (MPEP 2124). In the present application, Tat amino acid side chains are disclosed as being located at the R_1 and R_2 positions.

Therefore, it would be clear to the skilled artisan that R_1 and R_2 correspond to amino acid side chains including the basic-arginine rich region of HIV-1 Tat protein, and that this Tat basic region corresponds to HIV-1 Tat 49-57. In one embodiment, the side-chains correspond to SEQ ID NO:1 (new claim 29). However, the present invention is not limited to this embodiment. For example, Applicants disclose that the amino acid side-chains can correspond to SEQ ID NO:1 with a L-Tyr at the carboxyl-terminus (new claim 30). Also, Applicants disclose that the amino acid side chains can correspond to Tyr 47 to Arg 57 of HIV-1 Tat (page 11, line 27), which

corresponds to SEQ ID NO:1 with a L-Tyr at the amino-terminus (new claim 31). It is noted that only L-amino acids are found in proteins.

In summary, Applicants have shown possession of the invention by disclosure of structural chemical formulas, and other relevant identifying characteristics that would cause one of skill in art to immediately recognize that Applicants possessed the claimed invention as a whole. In view of the amendments and the remarks presented herewith, Applicants respectfully request withdrawal of these rejections.

Enablement Rejection

The Examiner has also rejected claims 1-5, 7-9, 16-19, 27 and 28 under 35 U.S.C. § 112, first paragraph, alleging that the specification does not reasonable enable a skilled artisan to practice the invention.

In particular, the Examiner states the following:

> **The disclosure appears to describe the preparation of a single compound comprising the oligourea set forth in Figure 1B wherein the side-chain substituents include the arginine-rich region of HIV-1 Tat as set forth in Figure 1A. Applicants may wish to amend the claim language to clearly set forth the chemical structure of the compound. The disclosure fails to provide adequate support for any other compounds and fails to provide any meaningful data pertaining to the in vivo and ex vivo activities of the compounds.**

The Examiner also alleges the following:

> **1) The claims encompass a large genus of compounds that are poorly described in the specification.**

2) The disclosure fails to provide sufficient guidance pertaining to the pharmacological profile of any of the Tat-derived oligourea derivatives.

3) The prior art teaches that the generation of successful HIV-1 antivirals is a difficult, complex, and often unpredictable process.

4) The disclosure fails to provide any in vivo or clinical working embodiments.

As stated above, Claim 1 is now directed to a synthesized oligourea comprising the recited structural chemical formula. As recited in claim 1, the oligourea molecule may vary in length from 3 to 50 urea-units long, and includes the basic-arginine rich region of HIV-1 Tat protein at the R_1 and R_2 positions. It is a universal fact that this Tat basic region corresponds to amino acids 49-57 of the naturally-occurring HIV-1 Tat protein, as mentioned above. Also, the claims now recite at least three examples of suitable amino acid side chain substitutions. For example, see new claims 29, 30 and 31, support for which can be found in the application as filed. Therefore, Applicants submit that the claims, as amended, provide significant structural requirements.

Contrary to the Examiner's assertions, the disclosure describes more than the preparation of a single compound. With reference to page 3, lines 22-34 and page 4, lines 1 and 2, the skilled artisan would immediately recognize that the synthesis procedure provided is suitable to synthesize any oligourea having the structural limitations recited in claim 1, not just a single oligourea derivative.

Furthermore, Applicants do not agree with the Examiner's allegations that the disclosure fails to provide any meaningful data pertaining to the *in vivo* and *ex vivo* activities of the compounds. In a response dated February 17, 2004, Applicants cited adequate support in the specification as filed, as well as working embodiments, for both *in vivo* and *ex vivo* applications.

For example, with respect to *in vivo* inhibitory methods, Applicants cited the transactivation assays shown in Figure 4 as evidence of a working example of an *in vivo* inhibitory method.

Applicants have shown that a compound of this invention inhibits binding of HIV-1 Tat to TAR RNA both *in vivo* and *in vitro*. Applicants have also disclosed other examples of oligourea compounds including the arginine-rich basic region of HIV-1 Tat protein, which have a reasonable expectation of success in interfering with Tat-TAR function given the known correlation in the art between the structure of the arginine-rich basic region of Tat (i.e., Tat 49-57) and its TAR RNA binding function. An oligourea of claim 1, when substituted with amino acid side chains modeled after a known nucleic acid binding domain will mimic the nucleic acid binding domain in specificity, but with a much lower disassociation constant (page 5, lines 29-33) of the application.

Given these facts, Applicants believe that the specification reasonably enables both *in vitro* and *in vivo* applications. However, in an effort to advance prosecution of the present invention, Applicants have amended the method of claim 2 to recite that the oligourea of claim 1 is introduced into a cellular environment in vitro. No further discussion with regard to the activities of the compounds is believed necessary in view of this amendment and the remarks presented herewith.

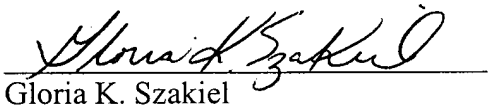
In view of the amended claims, and the arguments presented herewith, Applicants respectfully request withdrawal of these rejections.

Summary

Applicants submit that the claims, as presently recited, are patentably distinct over the art and allowable in form. An allowance of the claims is respectfully requested. Should the Examiner have any questions concerning this response, he is invited to contact the undersigned agent.

The commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account No. 08-2461.

Respectfully submitted,



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